## **ABSTRACT**

The present invention provides materials and methods which may be used to evaluate one or more different probes and select probes that are optimized for sensitivity and specificity for a particular target. In particularly preferred embodiments, the methods and compositions of the invention can be used to evaluate polynucleotide probes having different nucleotide sequences. The methods and compositions thereby allow a user to select a polynucleotide probe, *e.g.*, having a particular nucleotide sequence, that is optimized for sensitivity and/or for specificity for a particular target polynucleotide molecule. In particularly preferred embodiments, the methods and compositions can be used to evaluate a plurality of probes simultaneously, such as on a microarray.

Probes evaluated according to the methods of the invention can be selected for and used to detect a variety molecules, including a variety of of polynucleotides, such as genomic polynucleotides (e.g., genomic DNA) and genomic transcripts (e.g., mRNAs or cDNA sequences derived from there) as well as gene copy numbers of specific transcripts, single nucleotide polymorphisms, etc.

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